Appendices
Fig. 1. Normal squamous cells in Pap smear: Superficial cells are flattened, have abundant eosinophilic cytoplasm with a transparent quality, and pyknotic nuclei. Intermediate cells are folded, have less abundant cyanophilic or eosinophilic cytoplasm, and vesicular nuclei; nuclear-to-cytoplasmic (n:c) ratio is lower than that of parabasal cells. Normal parabasal cells are round-to-oval cells with dense basophilic cytoplasms and regular nuclei and are difficult to distinguish from squamous metaplastic cells (liquid-based ThinPrep; Papanicolaou stain).

Fig. 2. Normal endocervical cells: Appear en face as flattened honeycombed sheets of cells with finely vacuolated cytoplasm, round nuclei, and small nucleoli. On-edge the cells are columnar with basal, ovoid nuclei (liquid-based ThinPrep; Papanicolaou stain).
Fig. 3. **Squamous metaplasia**: Parabasal-type cells with variable shape, distinct cell borders, dense cytoplasm with cytoplasmic extensions, and rounded normochromic, regular nuclei with a relative increase in n:c (ThinPrep; Papanicolaou stain).

Fig. 4. **Normal endometrial cells**: Three-dimensional (3D) cluster of cells; nuclear size is comparable to intermediate cell nuclei and cytoplasm is scant (ThinPrep; Papanicolaou stain).
**Fig. 5. Lactobacilli:** Normal, rod-like organisms of the vaginal flora that maintain vaginal pH and produce cytolysis. "Bare" intermediate cell nuclei are seen (ThinPrep; Papanicolaou stain).

**Fig. 6. "Clue" cells:** Characteristic of bacterial vaginosis. Numerous small basophilic coccobacillary organisms cover the squamous cell surface (ThinPrep; Papanicolaou stain).
Fig. 7. *Candida albicans*: Shown with a shish-kebab effect. Mucus strands may mimic fungal organisms (ThinPrep; Papanicolaou stain).

Fig. 8. *Leptothrix*: Hair-like organisms commonly associated with *Trichomonas vaginalis* (ThinPrep; Papanicolaou stain).
**Fig. 9. Trichomonas vaginalis:** Pear-shaped organisms with an eccentric faint nucleus and cytoplasmic granules. Differential diagnosis includes degenerated nuclei and cytoplasmic debris (ThinPrep; Papanicolaou stain).

**Fig. 10. Herpes simplex virus:** Multinucleate giant cell with homogenous, "ground-glass" appearance of nuclei with margination of chromatin. Note nuclear molding. This infection is considered a medical emergency in pregnant patients (ThinPrep; Papanicolaou stain).
Fig. 11. Actinomyces: Associated with intrauterine device use. Filamentous organisms with clubbed peripheral ends are termed “Gupta bodies” (ThinPrep; Papanicolaou stain).

Fig. 12. Reactive/repairative squamous cells in Pap smear: May be seen in an inflammatory condition and are arranged in flat, cohesive sheets with a “streaming” effect (single cells are not seen), uniform slightly enlarged nuclei, a perinuclear halo, and small nucleoli. Repair may mimic nonkeatinizing squamous-cell carcinoma (ThinPrep; Papanicolaou stain).
Fig. 13. **Reactive endocervical cells:** Are in a honeycombed sheet with slight overlap, enlarged hyperchromatic nuclei, and prominent nucleoli (ThinPrep; Papanicolaou stain).

Fig. 14. **Radiation change:** Involves squamous and glandular cells, show enlarged cells with large nuclei, prominent nucleoli, abundant cytoplasm, nuclear and cytoplasmic vacuolation, multinucleation, intracytoplasmic inflammatory cells, and low n:c (conventional smear; Papanicolaou stain).
Fig. 15. **Intrauterine contraceptive device cells**: Are of endometrial origin. These cells appear singly with a high n:c ratio, nuclei may show atypia, and the cytoplasm is finely vacuolated (conventional smear; Papanicolaou stain).

Fig. 16. **Endometriosis**: Benign endometrial cells are present. Stromal cells and hemosiderin may also be seen (ThinPrep; Papanicolaou stain).
Fig. 17. "Exodus" (menstrual endometrium): Cluster of endometrial cells seen toward the end of menstruation and is comprised of glandular cells (at the periphery) and stromal cells (at the center) (ThinPrep; Papanicolaou stain).

Fig. 18. Atrophy: Flat sheet of basal and parabasal cell (ThinPrep; Papanicolaou stain).
Fig. 19. **Atrophic vaginitis**: Parabasal cells associated with numerous inflammatory cells, mummified parabasal cells “blue-blobs,” and granular background debris. The background debris is similar to tumor diathesis in squamous-cell carcinoma (conventional smear and ThinPrep; Papanicolaou stain).

Fig. 20. **Follicular cervicitis**: Polymorphous lymphoid cells and tingible-body macrophages—such changes may be associated with chlamydial infection or may be misinterpreted as malignant lymphoma or high-grade squamous intra-epithelial lesion (ThinPrep; Papanicolaou stain).
Fig. 21. Hyperkeratosis: Seen as a plaque of anucleate squames in a mucosal surface reaction in response to irritation. Although hyperkeratosis does not signify a squamous intra-epithelial lesion, it should be documented in the report, especially if extensive (HSIL) (ThinPrep; Papanicolaou stain).

Fig. 22. Parakeratosis: Another mucosal surface reaction characterized by the presence of miniature squamous cells. These cells exfoliate either singly or in aggregates (ThinPrep; Papanicolaou stain).
**Fig. 23. Tubal metaplasia:** Small strips of endocervical cells with cilia, terminal bars, and nuclear pseudostratification. It may originate from the upper endocervical canal, or may be misinterpreted as atypical glandular cells when cilia are lost during processing (conventional smear; Papanicolaou stain).
Fig. 24. **Endocervical polyp:** Numerous columnar endocervical cells with tubal metaplasia and spindled stromal cells may show slight nuclear atypia and may mimic adenocarcinoma in situ (AIS) (ThinPrep; Papanicolaou stain).

Fig. 25. **Syncytiotrophoblast:** Multinucleated giant cells usually seen in a postpartum smear, and may be mistaken for a high-grade malignancy (ThinPrep; Papanicolaou stain).
Fig. 26. **Atypical squamous cells of undetermined significance**: Mature cells with moderately enlarged nuclei (2.5–3 times the size of normal intermediate cell nuclei), minimal hyperchromasia, nuclear membrane irregularities, binucleation, and a mild increase in n:c. Atypical squamous cells of undetermined significance is distinguished from low-grade squamous intra-epithelial lesion (LSIL) on the basis of quality or quantity of cellular and nuclear changes (ThinPrep; Papanicolaou stain).

Fig. 27. **Low-grade squamous intra-epithelial lesion (LSIL)**. Please see legends to Figs. 28 and 24.
Fig. 28. LSIL (human papillomavirus [HPV] effect): Mature squamous cells with HPV effects—enlarged hyperchromatic nuclei with irregular envelope ("raisonoid") and binucleation. Cytoplasm has a sharply demarcated optically clear cytoplasmic (koilocytic) cavity (ThinPrep; Papanicolaou stain).

Fig. 29. LSIL (mild dysplasia): Nuclei are enlarged (more than three times the size of normal intermediate cell nuclei), hyperchromatic with mild nuclear membrane irregularity, and "mature" cytoplasm (ThinPrep; Papanicolaou stain).
Fig. 30. LSIL. Please see legend to Fig. 29 (ThinPrep; papanicolaou stain).
Fig. 31. **Atypical squamous cells cannot exclude HSIL.** Cells are of immature squamous metaplastic type. Nuclei are enlarged with slight membrane irregularity and hyperchromatic, finely granular chromatin. The n:c is not as high as HSIL (ThinPrep; Papanicolaou stain).

Fig. 32. **HSIL.** Parabasal- and metaplastic-type cells with high n:c and enlarged, hyperchromatic nuclei with marked nuclear membrane irregularity. The cytoplasm may be lacy or metaplastic in nature (ThinPrep; Papanicolaou stain).
Fig. 33. HSIL. Please see legend to Fig. 32 (ThinPrep; Papanicolaou stain).

Fig. 34. HSIL involving endocervical glands: Large syncytial aggregate (ill-defined cell borders) with loss of nuclear polarity. This may be misinterpreted as atypical glandular cells and is distinguished from it by lack of “feathering” and peripheral flattening of nuclei (ThinPrep; Papanicolaou stain).
Fig. 35. **Atypical parakeratosis**: Sheet of elongated miniature squamous cells with atypical nuclei, cytoplasm is eosinophilic to orangeophilic, and they may be associated with LSIL (ThinPrep; Papanicolaou stain).

Fig. 36. **Keratinizing dysplasia**: Shows both nuclear and cytoplasmic pleomorphism. Note the orange cytoplasm and large hyperchromatic nuclei (ThinPrep; Papanicolaou stain).
Fig. 37. Keratinizing squamous-cell carcinoma: Dispersed cells of spindle to elongated and caudate forms with heavily keratinized cytoplasm. Nuclei are pleomorphic and hyperchromatic, nucleoli are less conspicuous than the nonkeratinizing type, and tumor diathesis is generally lacking (conventional smear; Papanicolaou stain).

Fig. 38. Keratinizing squamous cell carcinoma. Please see legend to Fig. 37.
Fig. 39. Nonkeratinizing squamous-cell carcinoma: Malignant polygonal cells are arranged in either loose clusters, crowded groups, or singly. Nuclei are large, mostly round, and have coarse chromatin and macronucleoli. Cytoplasm is dense with distinct cell borders and high n:c. Tumor diathesis is generally present (ThinPrep; Papanicolaou stain).
**Fig. 40. Atypical glandular cells:** Overcrowded cluster of glandular cells showing large, variable and hyperchromatic nuclei with small nucleoli and scant cytoplasm (ThinPrep; Papanicolaou stain).

**Fig. 41. Atypical endocervical cells:** Two-dimensional sheet with focal palisading, “pseudo-feathering,” hyperchromatic nuclei, and nucleoli may be present (ThinPrep; Papanicolaou stain).
Fig. 42. **Atypical endometrial cells**: 3D cluster of cells with hyperchromatic nuclei, nucleoli, and scanty cytoplasm (ThinPrep; Papanicolaou stain).

Fig. 43. **Atypical endocervical cells, favor neoplastic**: Crowded sheet of atypical endocervical cells with nuclear overlap and focal "feathering" (ThinPrep and conventional smear; Papanicolaou stain).
Fig. 44. Endocervical AIS: “feathering” is the classic pattern of AIS and elongated hyperchromatic nuclei (ThinPrep; Papanicolaou stain).

Fig. 45. Endocervical AIS. Please see legend for Fig. 44.
Fig. 46. Endocervical AIS. Please see legend to Figs. 44 and 45 (conventional smear; Papanicolaou stain).

Fig. 47. Endometrial adenocarcinoma: 3D cluster with hyperchromatic nuclei, nucleoli, watery diathesis, and intracytoplasmic neutrophils (ThinPrep and conventional smear; Papanicolaou stain).
Fig. 48. Endometrial adenocarcinoma. Please see legend to Fig. 47 (Papanicolaou stain).

Fig. 49. Endometrial adenocarcinoma. Please see legend to Fig. 47 (ThinPrep; Papanicolaou stain).
Fig. 50. **Small-cell carcinoma of cervix:** Shows aggregate of small irregular tumor cells with scant cytoplasm and small nuclei. Nuclear molding is seen (ThinPrep; Papanicolaou stain).

Fig. 51. **Metastatic lobular carcinoma of breast:** Shows a cluster of small cells with large irregular nuclei and scant cytoplasm. Clean background of the smear is often observed in metastatic tumors. Clinical history is of extrauterine malignancy is important (ThinPrep; Papanicolaou stain).
Appendix 2
Suggested Readings


From: Fundamentals of Pap Test Cytology
By: R. S. Hoda and S. A. Hoda © Humana Press Inc., Totowa, NJ

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